Remarks

Claims 1-17 are pending in the present application. Claims 1-5, 8-10 and 15-16 are rejected under 35 USC §103(a) and Clams6-7, 11-14, and 17 or objected to as being dependent upon a rejected base claim but would be allowable if rewritten in independent form. Applicants respectfully request reconsideration of the application, withdrawal of all rejections, and allowance of the application in view of the amendments and remarks below.

The Amendments to the Claims

The amendments to the claims are believed to place the application in condition for allowance. Without prejudice to the Applicants' rights to present claims of equal scope in a timely filed continuing application, the Applicants have amended Claim 1 to expedite prosecution, provide clarity, and address the Examiner's concerns as expressed in the Office Action and as discussed further below. The amendments to the claims are supported by the specification and so are believed to be in condition for allowance.

The amendments to the claims do not introduce new matter. The Examiner is respectfully requested to enter the amendments to the claims and allow all claims.

The Rejection under 35 U.S.C. §103

The Examiner rejected Claims 1-5, 8-10, and 15-16 under 35 U.S.C. §103 as being unpatentable over Ingebrethsen (5,388,574). Office Action at page 2. According to the Office Action, "Ingebrethsen teaches an aerosol delivery article which provides delivery of aerosol particle of relatively small size without the necessity of exposing the aerosolized materials to a significant degree of heat or high temperature." *Id.* The Office Action further states that the first stage for aerosol particles of a fairly large size which are subjected to heat so as to vaporize the other ingredient of that aerosol and cause further dispersion of the first stage aerosol. The Office action further states that the heat is less than sufficient to cause vaporization of the active ingredient and the particles are less than about 5 micron and often less than about 1 micron. *Id.* at 2-3. The Office Action then goes on to state that although Ingebrethsen does not exemplify a method of preparing an aerosol of particles comprising the specific steps recited in claim 1, it does disclose all the elements and a general teaching of the method and thus it would have been obvious to modify the device of Ingebrethsen to provide aerosol particles of relatively small size. *Id.* at 3.

Applicants respectfully disagree in view of the amended claim 1 and the disclosures of. Ingebrethsen. As amended above, Claim 1 is directed to a method for forming a drug condensation aerosol with a MMAD of less than 0.1 μm, wherein the condensation aerosol is formed by vaporizing the drug and mixing it with a gas in a ratio to form the desired particle size..

Ingebrethsen does not teach vaporization of the drug or active ingredient. Ingebrethsen actually teaches away from the instant invention. Ingebrethsen teaches an aerosol device that generates a first aerosol using a nebulizer. These nebulized particles are then heated to form smaller particles, but to a temperature less than "sufficient to cause vaporization . . . of the active ingredient." U.S. Patent 5,388,574, Abstract & Column 2. The Ingebrethsen device is evaporating or vaporizing off a non-active component having a low-vaporization temperature from the active component. *Id.* Ingebrethsen specifically teaches away from the Applicants' invention by requiring that the heat to disperse the first stage aerosol be less than that sufficient to cause vaporization of the active ingredient. Applicants' invention is directed to aerosols and methods of producing aerosols that vaporize the "active ingredient" or drug.

Additionally, Ingebrethsen does not enable aerosol particles of less than 0.1 μm or teach the criticality of this size. While Ingebrethsen mentions that "the mass average size of the aerosol particles of the second stage aerosol is less than about 5 μm, often is less than about 3 μm, and frequently is less than about 1 μm," he also states "[t]ypically, the mass average size of the aerosol particles of the second stage aerosol is at least about 0.2 μm, and often at least about 0.5 μm." (col. 11, lines 29-34). Thus, Ingebrethsen does not disclose or teach aerosols with MMADs as set forth in amended Claim 1. Additionally, Ingebrethsen does not disclose the criticality of the less than 100 nm particles size relative to the .02 to 5 μm particle range. The claimed aerosol particle size of less than 100 nm is critical for effective drug delivery through diffusion and achieves unexpected results relative to the .02 to 5 μm range. Applicants not only enable one to make aerosols having particle sizes of less than 0.1 μm, but also teach the criticality of this particle size. Applicants specifically teach that ultra fine particles of less than 100 nm are sufficiently small so as to diffuse in the lung in a timely manner. In contrast, Applicants teach that particles "between 0.1 and 1 micron in size, are too small to settle onto the lung wall and too massive to diffuse to the wall in a timely manner. Thus, a significant number of such particles are removed from the lung by exhalation, and . . . are not involved in treating disease." U.S. 2003/0062042 A1 (Appl. No. 10/057,197) [0017](incorporated by reference in the instant application). A showing of the criticality of a range relative to the prior art can be used to rebut a prima facie case of obviousness based on overlapping ranges. See, *e.g., In re Woodruff,* 919 F.2d 1575, 16 USPQ2d 19334 (Fed. Cir.

1990). As the Ingebrethsen reference does not enable aerosol of MMADs of less than 0.1 μm as claimed in the instant invention and this particle size is critical to drug diffusion in the lung, this reference can not make obvious the claimed invention.

According to the MPEP § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations." Obviousness cannot be established by combining teachings in the prior art, absent some teaching or suggestion in the prior art that the combination be made (*In re Stencel* 828 F. 2d 751, 4 USPQ2d 1071 (Fed. Cir. 1987); *In re Newell* 891 F. 2d 899, 13 USPQ2d 1248 (Fed. Cir. 1989)).

As the Ingebrethsen reference does not teach or suggest all the claim elements, but rather teaches away from the claimed invention, Ingebrethsen does not make obvious the instant invention. Moreover for the same reason, there would be no motivation to modify Ingebrethsen's device to achieve the presently claimed invention. As Claims 4-5, 8-10, and 15-16 depend from Claim 1, Claims 4-5, 8-10, and 15-16 are not obvious for the same reasons.

The Examiner has rejected Claims 1-4under 35 U.S.C 103(a) as being unpatentable over Faithfull et al (6,041,777). Office Action at page 3. The Office Action states in summary that Faithfull teaches methods and apparatus for closed-circuit ventilation therapy, including the use of nebulizers to provide flurochemicals and/or pharmaceutical agents, heated above body temperature, to a ventilating gas in the form of a vapor and that this is accomplished by spraying or contacting a wetted surface or wick with the gas to form droplets. *Id.* Thus, according to the Office Action although Faithfull does not exemplify a method of preparing an aerosol of particles comprising the specific steps recited in claim 1, it does disclose all the elements and a general teaching method.

Applicants respectfully disagree in view of the disclosure of Faithfull. Faithfull does not disclose or teach a condensation particle or aerosol as defined by the Applicants' claims or how to make such an aerosol. Faithfull discloses the use of a warmed fluorochemical as a solvent for delivering the active compound "oxygen" to the lungs of the patient using a ventilation system. The active or therapeutic compound or drug in Faithfull is not vaporized and subsequently condensed into aerosol particles, as is set forth in Claim 1 of the instant application. Additionally, there is no teaching in Faithfull of producing a drug condensation particle by passing air through the heated vapor. Rather, Faithfull teaches away from such a condensation particle, as oxygen gas is already being passed through

the system described by Faithfull and no condensation particle is formed. Instead, Faithfull requires the use of a wetted surface or wick to get the fluorochemical (solvent) to form a droplet. Moreover, as was stated in the Office Action, the fluorochemical in the Faithfull reference, unlike the present invention, is being delivered to the lung as a vapor and not an aerosol. (See Office Action at 4, "as the fluorochemical vapor cools in the body it is deposited on the pulmonary surfaces." (Emphasis added)). Faithfull does not disclose how to make a condensation aerosol or how to obtain MMAD sizes of less than 0.1 μm for condensation aerosols. Accordingly, the Office Action fails to establish even a *prima facie* case of obviousness as each and every element of the invention is not taught or disclosed by Faithfull.

Claims 2-4 which depend from Claim 1 patentably define Faithfull for the same reasons that Claim 1 does.

Claims 6-7, 11-14, and 17 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form. In view of the arguments set forth and the amendment to Claim 1, Applicants believe that these claims are in condition for allowance as written.

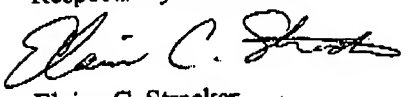
Accordingly, and in light of the foregoing arguments, the Applicants respectfully submit that these amendments put the case in condition for allowance and request that the Examiner reconsider and withdraw all rejections based on 35 U.S.C §103.

Conclusion

The Applicants appreciate the Examiner's careful and thorough review of the application and submit that the Examiner's concerns have been addressed by the amendments and remarks above. The Applicants accordingly request the Examiner to withdraw all rejections and allow the application. In the event the Examiner believes a telephonic discussion would expedite allowance or help to resolve outstanding issues, prosecution of the application, then the Examiner is invited to call the undersigned at (650) 687-3905. Please direct all correspondence to the following customer number: 37485.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 502731.**

Respectfully submitted,



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